UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,492	01/07/2002	Adriana Silva Hemerly	217943US0X CONT	3581

45473 7590 07/01/2005

HUTCHISON & MASON PLLC
PO BOX 31686
RALEIGH, NC 27612

EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,492	HEMERLY ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *129-215* is/are pending in the application.

4a) Of the above claim(s) *145 and 171* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *129-144,146-170 and 172-215* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.A

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed March 7, 2005 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 7, 2005 has been entered.

Claims 1-128 are cancelled.

Claims 129-215 are newly added.

Claims 129-215 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Election/Restrictions

Newly submitted claims 145 and 171 are directed to an invention that is independent or distinct from the invention originally elected for the following reasons: newly submitted claims 145 and 171 require the use of a vector comprising a nematode-induced promoter operably linked to the claimed DNA sequences, whereas the invention originally elected required only the use of a promoter functional in plants cells. A nematode-induced promoter is structurally distinct from a promoter that is generally functional in plants cells because a nematode-induced promoter contains structural motifs

not found in promoters that are generally functional in plants cells. A nematode-induced promoter is functionally distinct from a promoter that is generally functional in plants cells because a nematode-induced promoter functions only upon nematode induction whereas a promoters that is generally functional in plants cells is presumed to function more or less constitutively. Accordingly the use of a vector comprising a nematode-induced promoter operably linked to the claimed DNA sequences would require an additional search specifically directed to nematode-induced promoters and their use in plant cells.

Since applicant has received an action on the merits for the originally elected invention, prosecution on the merits is limited to this invention. Accordingly, claims 145 and 171 are withdrawn from consideration as being directed to a non-elected invention.

Regarding the previous Restriction Requirement, Applicants point out that Claim 48 corresponds to newly-added Claim 145. Claim 143 ultimately depends from Claim 129. Applicants maintain that since Claim 129 is allowable, it is irrelevant that that Claim 145 contains additional subject matter, and that the dependent claim is patentable for the same reasons as the independent claim from which it depends. Similarly, Claim 171 ultimately depends from Claim 129, which is allowable. Applicants therefore maintain that the rejoinder provisions of MPEP 821.04 apply to Claims 145 and 171, and that Accordingly, those claims should be rejoined with the elected subject matter. (reply page 21)

The Examiner also maintains that the rejoinder provisions of MPEP 821.04 do not apply to the instant situation. The rejoinder provisions of MPEP 821.04 allow for rejoinder of product claims with claims directed to methods of making and using the

claimed products. The rejoinder provisions of MPEP 821.04 apply where applicant is called upon under 35 U.S.C. 121 to elect claims to either a product or a process and applicant elects claims directed to the product and a product claim is subsequently found allowable, or where the application as originally filed discloses the product and the process for making and/or using the product, and only claims directed to the product are presented for examination. Neither situation is applicable here, as both product and process claims were elected and examined. Further, it is relevant where an allowed claim contains additional subject matter, as the rejoinder provisions of MPEP 821.04 also provide that in the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104, and that thus to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. This provision, however, is inapplicable to the instant application, as both product and process claims were elected and examined.

Claim Objections

Claims 141-142 and 164-165 are objected to because of the following informalities: the claims are directed in part to a nonelected sequence (SEQ ID NO: 9). Appropriate correction is required.

Applicants maintain that the objection to the claims is believed to be obviated by the amendment submitted above in part and is in part respectfully traversed. Regarding Claims 41-45 and 70-74, which correspond to newly-added claims 141-142 and 164-165, just because one sequence has been elected does not forbid a dependent claim from specifying another sequence. Specifically, the elected sequence defines an amino acid

sequence, and SEQ ID NO: 9 is a DNA sequence which encodes that amino acid sequence. Applicants also maintain that the dependent claims are allowable for the same reasons as the independent claim, and that accordingly, the rejoinder provisions of MPEP 821.04 apply to the subject matter of Claims 41-45 and 70-74. Accordingly, withdrawal of he objections is respectfully requested. (reply pages 20-21)

The Examiner maintains that the claims were properly objected to for reciting a nonelected sequence (SEQ ID NO: 9) which had previously been withdrawn from consideration as being directed to a nonelected invention. The originally elected invention of Group VII and SEQ ID NO:6 was directed to a DNA vector comprising a non-genomic DNA sequence coding for a protein or peptide comprising an amino acid sequence of SEQ ID NO:6 or an amino acid sequence having at least 50% amino acid sequence identity thereto, or a DNA sequence having at least 75% nucleotide sequence identity to said non-genomic DNA sequence, operably linked to a promoter functional in plant cells. The coding sequence of SEQ ID NO:9 was encompassed by the nonelected invention of Group V, original claims 10-13, drawn to a non-genomic DNA sequence encoding a protein or a peptide, which group was directed in part to the DNA sequence given as SEQ ID NO:9 (original claim 12). The inventions of claims 1-9, 12-13, 16 and 22, and the nonelected sequences were withdrawn from consideration as being directed to nonelected inventions at page 4 of the office action mailed April 13, 2004. Furthermore, the search of the sequence of the elected invention did not encompass a search of the nonelected sequence, as the sequence of the elected invention, SEQ ID NO:6, is a sequence of 24 amino acids, whereas SEQ ID NO:9 is a sequence of 2434 nucleotides

that encodes a sequence of 728 amino acids in length (the nonelected sequence of SEQ ID NO:5).

The Examiner also maintains that the rejoinder provisions of MPEP 821.04 do not apply to the instant situation. The rejoinder provisions of MPEP 821.04 allow for rejoinder of product claims with claims directed to methods of making and using the claimed products. The rejoinder provisions of MPEP 821.04 apply where applicant is called upon under 35 U.S.C. 121 to elect claims to either a product or a process and applicant elects claims directed to the product and a product claim is subsequently found allowable, or where the application as originally filed discloses the product and the process for making and/or using the product, and only claims directed to the product are presented for examination. Neither situation is applicable here, as both product and process claims were elected and examined.

Claim Rejections - 35 USC § 112

Claims 129-144, 146-170 and 172-215 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record.

Applicant's arguments filed March 7, 2005 have been fully considered but they are not persuasive.

Applicants maintain that claim 129 defines the protein of the present invention and defines the structure and the function of the inventive protein in detail. Applicants

point out that the claim specifies that the protein is a cdc27 protein and that its amino acid sequence contains SEQ ID NO: 6 or a sequence having at least 50% sequence identity to SEQ ID NO: 6 contained in a stretch of 161 NH2-terminal amino acids. Applicants point out that claim 129 even explicitly requires that the NH2-terminal domain is conserved in cdc27 homologues of different origin, and that an intact tetratricopeptide domain is also specified. In terms of function, Applicants point out that claim 129 specifies that the protein is capable of modulating DNA replication in plant cells. (reply pages 14-15)

Applicants' comments are inapposite to the outstanding rejection. The outstanding rejection was not predicated on the failure of the claims to define the structure and the function of the inventive protein in detail. The outstanding rejection was predicated of the failure of the specification to describe the claimed invention.

Applicants also point out that they have conducted a BLAST search using SEQ ID NO: 6, and a copy of the results of the BLAST search are submitted herewith. Applicants point out that all hits obtained in the search having at least 50% sequence identity to SEQ ID NO: 6 are cdc27 proteins, and maintain that even though SEQ ID NO: 6 is a relatively short sequence, it is sufficient to identify cdc27 proteins and nothing else. (reply page 15)

The Examiner maintains that the issue with respect to written description is not whether SEQ ID NO: 6 or a sequence having at least 50% sequence identity thereto is sufficient to identify cdc27 proteins, but whether the specification adequately describes cdc27 proteins comprising SEQ ID NO: 6 or a sequence having at least 50% sequence identity thereto. In this regard the Examiner notes that Applicants have not correlated the

BLAST search submitted with sequences described in the instant disclosure and/or publicly available at the time of filing. The sequences set forth in the BLAST search submitted in fact do not appear to have been available at the time of filing, the time at which the written description requirement must be satisfied, as a search of SEQ ID NO:6 did not identify any prior art sequences. In this regard the Examiner maintains that sequences published after the filing date of the instant application cannot be used to support the written description of the claimed sequences, as the written description requirement must be satisfied at the time of filing.

Applicants additionally point out that the specification of the present application explicitly states that the function of the tetratricopeptide (TPR) domains is to enable the protein to interact with other proteins in the APC, and that the specification further states that mutation analysis in the TPR domains of yeast cdc27 revealed that intact TPRs are necessary for cdc27 function and for a functional APC. Applicants also point in particular to the specification at paragraph [0021] which states that SEQ ID NO: 6, and thus also SEQ ID NO:10 are part of a unique NH2-terminal domain conserved in CDC27 homologues of different origin. Applicants point out that SEQ ID NO:10 is in fact the stretch of 161 NH2-terminal amino acids specified in Claim 129, and Applicants also point in particular to paragraph [0017] states the novel exon encoded by amino acid sequence SEQ ID NO: 6 is part of a unique NH2-terminal domain conserved in CDC27 homologues of different origin. Reference to sequences having at least 50% identity to SEQ ID NO: 6 may be found in, for example, paragraph [0009]. Applicants maintain that there is thus ample support in the application as filed for an NH2-terminal domain

conserved in cdc27 homologues of different origin comprising a stretch of 161 NH2-terminal domain amino acids and comprising SEQ ID NO: 6 or a sequence having at least 50% identity thereto. Accordingly, Claim 129 is supported by the disclosure, and is not new matter. (reply pages 15-16)

The Examiner acknowledges that the specification discloses at [0021] SEQ ID NO 6, and thus also SEQ ID NO 10, are part of a unique NH.sub.2-terminal domain conserved in CDC27 homologues of different origin. The Examiner maintains, however, that an isolated DNA sequence encoding a cdc27 protein wherein the protein comprises an NH_2-terminal domain comprising a stretch of 161 NH_2-terminal amino acids that comprises an amino acid sequence having at least 50% to 98% identity to SEQ ID NO:6 wherein the protein comprises an intact tetratricopeptide domain does not find support in the specification as originally filed, and thus constitutes new matter. The reference to sequences having at least 50% identity to SEQ ID NO: 6 found in paragraph [0009] is not made in reference to an isolated DNA sequence encoding a cdc27 protein wherein the protein comprises an NH_2-terminal domain comprising a stretch of 161 NH_2-terminal amino acids that comprises an amino acid sequence having at least a % sequence identity to SEQ ID NO: 6 . The reference to sequences having at least 50% identity to SEQ ID NO: 6 found in paragraph [0009] provides

> The present invention therefore relates in the first place to an at least partially purified protein, capable of modulating DNA replication in plants, at least comprising in the amino acid sequence
>
> a) one or more of the amino acid sequences chosen from the group consisting of those, given by SEQ ID NOS 2, 3 and 4,
>
> b) one or more of the amino acid sequences chosen from the group consisting of those, given by SEQ ID NOS 6, 7, 10 and 12.

c) one or more amino acid sequences having at least 50% amino acid identity with those of a), or

d) one or more amino acid sequences having at least 50% amino acid identity with those of b).

Applicants additionally maintain that there are at least three examples of sequences that fall within the scope of Claim 129 described in the present specification. Those sequences are SEQ ID NO: 6 (which encodes cdc27A1 protein), SEQ ID NO: 14 (which encodes cdc27A2 protein), and SEQ ID NO: 15 (which encodes cdc27B protein). As can be seen in the alignment presented in Figure 6 of the present application, the proteins encoded by those sequences comprise SEQ ID NO: 6 or a peptide having at least 50% amino acid identity with SEQ ID NO: 6. Applicants maintain that the specification of the present application thus describes multiple species within the genus embraced by Claim 129. (reply page 16)

With respect to Applicant's assertion that the specification of the present application describes multiple species within the genus embraced by Claim 129, the Examiner maintains that the disclosure of three different nonelected sequences obtained from a single species of organism is not a representative number of species sufficient to support the description of the broadly claimed genus which encompasses isolated DNA sequences obtained from any unspecified source that encode cdc27 proteins that comprise the 24 amino acid residue domain of SEQ ID NO:6 or that comprise an amino acid sequence having more than 50% identity to the 24 amino acid residue domain of SEQ ID NO:6.

Applicants also maintain that in addition, there is an implicit disclosure of more sequences because, based on the knowledge of explicitly described cdc27 sequences, one could isolate equivalent genes from other plant species using routine experimentation. Applicants maintain that it was known at the time the present application was filed that those equivalent genes may have some sequence variation, and that it would be recognized that isolation of such equivalent genes from other plant species is routine once the sequence of the Arabidopsis genes are known, i.e., based on the sequences described in the present application one can readily isolate the orthologue from another plant species. (reply page 16)

With respect to Applicant's assertion that there is an implicit disclosure of more sequences because, based on the knowledge of explicitly described cdc27 sequences, one could isolate equivalent genes from other plant species using routine experimentation, the Examiner maintains that one's ability to isolate equivalent genes from other plant species using routine experimentation does not describe the sequences of those equivalent genes. Whether a sequence is described is not dependent on whether the specification provides an enabling disclosure. See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), which discusses the description of a claimed human cDNA sequence based on the disclosure of a rat cDNA sequence and a method for obtaining the human cDNA sequence:

> The patent describes a method of obtaining this cDNA by means of a constructive example, Example 6. This example, however, provides only a general method for obtaining the human cDNA (it incorporates by reference the method used to obtain the rat cDNA) along with the amino acid sequences of human insulin A and B chains. Whether or not it provides an enabling disclosure, it does not provide a written description of the cDNA encoding human insulin, which is necessary to provide a written description of the subject matter of claim 5. The

> name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. (*Lilly*, 43 USPQ2d at 1405)

With respect to the Examiner's citation of the Lilly decision at page 7 of the prior Official Action, Applicants maintain that the facts of the present application are very different from the situation in Lilly. Applicants point out that the specification described a rat cDNA sequence and described a method of obtaining a human CDNA sequence. Significantly, the specification did not describe the actual sequence of the human CDNA. For that reason, a claim to the human CDNA was found to lack written description in the specification. However, in the present application, all of the features of Claim 129 are described, as discussed above. In particular, the results of the BLAST search submitted herewith demonstrates that SEQ ID NO: 6 or a sequence having at least 50% sequence identity thereto is sufficient to identify cdc27 proteins. (reply pages 16-17)

Applicants comments are inapposite to the Examiner's citation of the Lilly decision at page 7 of the prior Official Action, as the Examiner's citation of the Lilly decision at page 7 of the prior Official Action were directed solely to Applicants comments regarding Applicant's assertion that there is an implicit disclosure of more sequences because, based on the knowledge of explicitly described cdc27 sequences, one could isolate equivalent genes from other plant species using routine experimentation.

The Examiner also reiterates that the issue with respect to written description is not whether SEQ ID NO: 6 or a sequence having at least 50% sequence identity thereto is

sufficient to identify cdc27 proteins, but whether the specification adequately describes cdc27 proteins comprising SEQ ID NO: 6 or a sequence having at least 50% sequence identity thereto. In this regard the Examiner notes that Applicants have not correlated the BLAST search submitted with sequences described in the instant disclosure and/or publicly available at the time of filing. The sequences set forth in the BLAST search submitted in fact do not appear to have been available at the time of filing, the time at which the written description requirement must be satisfied, as a search of SEQ ID NO:6 did not identify any prior art sequences. In this regard the Examiner maintains that sequences published after the filing date of the instant application cannot be used to support the written description of the claimed sequences, as the written description requirement must be satisfied at the time of filing.

Claims 129-144, 146-170 and 172-215 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record.

Applicant's arguments filed March 7, 2005 have been fully considered but they are not persuasive.

Applicants traverse the rejection and maintain that the present specification provides a detailed description of how to make and use the DNA sequence recited in Claim 129 so that the scope of the invention can be practiced without undue experimentation. Applicants point in particular to Example 4 at pages 37-39 of the

specification, which provides ample guidance on which elements of the sequence may be modified and which elements might give rise to alteration in function/activity. Applicants submit that the claimed nucleic acids are isolatable from genomic libraries by routine methods, and that based on the sequences of the present invention it was possible to isolate a true cdc27 protein, without undue experimentation for the skilled person, because this isolation can be done by routing experiments like hybridization or PCR. (reply pages 17-18)

The Examiner maintains that Example 4 at pages 37-39 of the specification does not enable the elected invention as Example 4 is directed to the use of sequences nonelected in the reply filed January 16, 2004 (CDC27 muteins). The Examiner also maintains that the outstanding rejection was not predicated on the failure to provide guidance with respect to the general use of techniques that are known to and within the abilities of one skilled in the art. The outstanding rejection was predicated on the failure to provide guidance with respect to how to make and use sequences having the structural and functional attributes recited in the claims. Such guidance is necessary because it is unpredictable whether and how a CDC27 protein comprising an NH2-terminal domain comprising a stretch of 161 NH2-terminal amino acids wherein the stretch comprises SEQ ID NO:6 or an amino acid sequence having at least 50% to 98% identity to SEQ ID NO:6 wherein the protein comprises an intact tetratricopeptide domain would modulate DNA replication or promote anaphase promoting complex-substrate action in plant cells. It is unpredictable because the function of SEQ ID NO:6 and its corresponding domain in other CDC27 proteins is unknown. It is also unpredictable because cdc27 proteins are

known to require more than one domain for function, and because different types of tetratricopeptide domains may exhibit different functions.

The specification teaches that the CDC27 protein is known in the art to be a part of a high molecular weight complex referred to as the anaphase promoting complex (APC) or cyclosome, which in yeast is composed of at least 8 different proteins (page 2). The specification also teaches that it is known in the art that the APC functions to target substrates for proteolytic degradation by catalyzing the ligation of ubiquitin to the substrates, resulting in the restriction of DNA replication to occur only once during the cell cycle (pages 2-3). The specification additionally teaches that it is known in the art that at least CDC16, CDC23 and CDC27 require phosphorylation in the M-phase for activation (page 2 lines 37-39). The specification further teaches that the CDC27A1 exon encoding the amino acid sequence SEQ ID NO:6 corresponds to a CDC27 N-terminal domain whose role is not currently known (page 6 lines 3-29). Since the role of the CDC27 domain corresponding to SEQ ID NO:6 is unknown, and since CDC27 is known to require both the presence of other proteins as well as phosphorylation for activation, which suggests that CDC27 comprises multiple distinct functional domains, it is unpredictable what specific function or effect would be exhibited by a CDC27 protein comprising an NH2-terminal domain comprising a stretch of 161 NH2-terminal amino acids wherein the stretch comprises SEQ ID NO:6 or an amino acid sequence having at least 50% to 98% identity to SEQ ID NO:6 wherein the protein comprises an intact tetratricopeptide domain.

See also, for example, for example, Lamb J.R. et al. (Tetratrico peptide repeat interactions: to TPR or not to TPR? Trends Biochem Sci. 1995 Jul;20(7):257-9. Review),

who teach that different tetratrico peptide repeats may mediate different functions, even within the same protein. Lamb J.R. et al. teach that a mutation within TPR7 of CDC27 reduces its ability to interact with CDC23, but does not affect its interactions with CDC16 or itself, implying that TPR7 of CDC27 mediates interactions with CDC23, and that other interactions are mediated by other regions of CDC27, perhaps other TPRs (page 258 column 1). Since different CDC27 tetratrico peptide repeats may mediate different specific functions, it is unpredictable what specific function or effect would be exhibited by a CDC27 protein comprising an NH2-terminal domain comprising a stretch of 161 NH2-terminal amino acids wherein the stretch comprises SEQ ID NO:6 or an amino acid sequence having at least 50% to 98% identity to SEQ ID NO:6 wherein the protein comprises an intact tetratricopeptide domain.

In the instant case the specification does not provide sufficient guidance with respect to how to make and use isolated DNA sequences encoding a CDC27 protein that comprises an NH2-terminal domain comprising a stretch of 161 NH2-terminal amino acids wherein the stretch comprises SEQ ID NO:6 or an amino acid sequence having at least 50% to 98% identity to SEQ ID NO:6 wherein the protein comprises an intact tetratricopeptide domain and wherein the protein, when expressed in a plant cell, has a specific effect on DNA replication or anaphase promoting complex-substrate action. Absent such guidance, one skilled in the art would have to test each of the myriad of CDC27 protein coding sequences encompassed by the claims for its specific effect on DNA replication or anaphase promoting complex-substrate action in a plant cell or plant transformed therewith in order to discriminate between those sequences that function as

desired and those that do not. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

In response to the Examiner's concern that the effect of a peptide having only 1 exon (SEQ ID NO 6) is unpredictable, claim 129 specifies that the protein comprises SEQ I.D NO: 6 and is capable of modulating DNA replication in plant cells, said recitation being supported by the specification at page 6, lines 23-25, which states that the presence of exon SEQ ID NO: 6 is responsible for promoting Apc-substrate action and DNA replication. Applicants maintain that said recitation is further supported by the common knowledge that the N-terminus of cdc27 proteins harbors the highly conserved in CDC27/NUC2-LIKE domain, of which SEQ ID NO 6: is a large portion. Applicants therefore submit that the effect of the presence of SEQ ID NO: 6 is a functional effect of the protein, which functional effect is to the promote APC substrate action and therewith DNA-replication. With respect to "undue experimentation", Applicants maintain that the specification provides guidance to use proteins comprising SEQ ID NO: 6, which is part of a stretch of at least 161 amino acids, which is part of a cdc27 domain and which is part of a protein with the biological function of modulating DNA replication, and that no undue experimentation is necessary, since the presence of SEQ ID NO: 6 is related to the biological function of the protein as it contributes to APC substrate activity and therewith in DNA replication. (reply page 18)

The Examiner maintains that the description of a protein's function as "capable of modulating DNA replication" and promoting or contributing to "APC substrate activity" do not provide guidance for enabling the claimed invention as modulating DNA

replication and promoting or contributing to APC substrate activity are not specific activities of a protein. The Examiner also maintains that the presence of SEQ ID NO: 6, or an amino acid sequence having at least 50% identity thereto, is not known or disclosed as being necessary and sufficient to confer DNA replication modulating activity or APC-substrate action promoting activity to a protein. With respect to the functionality of SEQ ID NO: 6, the Examiner reiterates that specification at page 6 in fact states that "the role of this domain is not currently known, but its conservation suggests that it is indispensable of CDC27 function" and that proteins comprising this novel exon sequence "may promote APC-substrate action and therewith allowing DNA-replication". The specification does not, however, disclose a specific function for SEQ ID NO: 6 or provide specific guidance with respect to how to use SEQ ID NO: 6 to achieve a specific function or a specific effect.

Applicants also maintain that the other Examples of the present application also provide explicit teaching for making and using the claimed DNA sequence. Applicants point to in particular to Example 2, which describes the isolation of the cdc27A1 gene, which is an example of a sequence which comprises SEQ ID NO: 6 and is capable of modulating DNA replication in plant cells. Applicants point to Example 5 which relates cdc7, and is relevant for the description of the cloning steps and vectors, which are referred to in the Examples which relate to SEQ ID NO: 6. Applicants point to Example 6 which is a prophetic example of how to obtain male sterility in plants using a cdc27 protein which is mutant and which is cloned under control of a tapetum specific example and therefore disrupts cell division. Applicants point to Example 7 which is a

hypothetical example which describes that the cdc27 muteins can be used to increase endoreduplication as mentioned in Example 4. Example 7 provides additional details on how to clone the mutants and to transform them into plants. Applicants point to Example 8 describes a study of the natural expression occurrence of the cdc27 protein, which comprises SEQ ID NO: 6. Applicants point to Example 9 describes cloning a gene encoding a cdc27B protein, which comprises SEQ ID NO: 6. Applicants point to Example 10 describes the cloning of cdc27B protein, which comprises a peptide that is at least 50% identical to SEQ ID NO: 6. (reply pages 18-19)

In addition, Applicants point out that they have also conducted the following experiments. Tobacco plants were transformed with a 35S::Atcdc27A1 construct, and these plants showed improved characteristics (or improved or useful phenotypes) such as improved growth characteristics, which is manifested by improved yield, improved plant height and improved biomass. See Figure 2 submitted with the response filed on July 20, 2004. In addition, more cell division, which is manifested by more branching was also observed (see Figure 2). The plants transformed plants also had more leaves as shown in Figure 3 attached hereto and bigger leaves as shown in Figure 4 submitted with the response filed on July 20, 2004. Transformation of Arabidopsis with cdc27B Arabidopsis plants were transformed with a 35S::Atcdc27B construct and them resulting plants showed improved characteristics (or improved or useful phenotypes) such as improved growth characteristics manifested by stay-green phenotype. See Figure 5 submitted with the response filed on July 20, 2004. Figure 5 also shows that the transformed cells had more cell division as manifested by more branching and more leaves. (reply pages 19-20)

The Examiner maintains that the examples cited by Applicants are not commensurate in scope with the elected invention. The examples cited by Applicants are directed to the use of sequences nonelected in the reply filed January 16, 2004 (muteins, SEQ ID NOS: 5 and 9=CDC27A1, SEQ ID NOS: 11 and 14=CDC27A2, and SEQ ID NOS: 13 and 15=CDC27B) and withdrawn from consideration in the office action mailed April 13, 2004. While these examples are relevant to the extent that they support the functionality of the domain of SEQ ID NO: 6 in the context of a full-length CDC27 protein, the examples do not provide guidance with respect to how to make and use sequences encoding CDC27 proteins that comprise an amino acid sequence having at least 50% to 98% sequence identity to SEQ ID NO: 6.

Claims 129, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 129 is indefinite in the recitation of "capable of". It is unclear whether claim in fact requires that the protein modulate DNA replication in plant cells.

Claims 129, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 129 is indefinite in the recitation of "modulating DNA replication in plant cells". It is unclear what the protein does with respect to DNA replication in plant cells, as the term "modulate" is not

a specific activity of a protein, and the specific activity cannot be discerned by the structural limitations recited in the claims.

Claims 130 and 156, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants maintain that the rejection of the claims under 35 U.S.C. 112, second paragraph, is believed to be obviated by the amendments submitted above, and that in the newly-added claims, the language identified by the Examiner has either been modified or the subject matter of the claim is not recited therein (reply page 20).

The Examiner maintains that the newly submitted claims are indefinite in the recitation of "promotes anaphase promoting complex-substrate action". It is unclear what the protein does with respect to anaphase promoting complex-substrate action, as the term "promote" is not a specific activity of a protein, and the specific activity cannot be discerned by the structural limitations recited in the claims. It is also unclear what type of action is promoted, as more than one type of action may occur between a substrate and other proteins, such as binding or catalytic action.

Claim 156, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants maintain that the rejection of the claims under 35 U.S.C. 112, second paragraph, is believed to be obviated by the amendments submitted above, and that in the

newly-added claims, the language identified by the Examiner has either been modified or the subject matter of the claim is not recited therein (reply page 20).

The Examiner maintains that the newly submitted claim is indefinite in the recitation of "allows DNA replication". It is unclear what the protein does with respect to DNA replication, as the term "allows" is not a specific activity of a protein, and the specific activity cannot be discerned by the structural limitations recited in the claims.

Claim 174, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants maintain that the rejection of the claims under 35 U.S.C. 112, second paragraph, is believed to be obviated by the amendments submitted above, and that in the newly-added claims, the language identified by the Examiner has either been modified or the subject matter of the claim is not recited therein (reply page 20).

The Examiner maintains that the newly submitted claim is indefinite in the recitation of is indefinite in the recitation of "modifying the characteristics". It is unclear what characteristics are modified, as plant cells and plants exhibit a plethora of different characteristics, whereas transformation of a plant cell or plant with a particular coding sequence would be expected to modify only a specific subset of these characteristics. It is also unclear in what way the characteristics are modified, as any given characteristic may be modified in different ways, whereas transformation of a plant cell or plant with a particular coding sequence would be expected to result in specific types modifications for specific characteristics.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Examiner
Art Unit 1638

CC

Cynthia Collins
6/27/05